Tissue specificity of decellularized rhesus monkey kidney and lung scaffolds.

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Public Summary:
The first goal of these studies was to characterize the contents that remain after removal of cells using a decellularization process to obtain the natural templates of the kidney or lung. These studies are important because attempts to recellularize donor tissues that may have elements that remain after the decellularization process could result in an immune response post-transplantation. These studies also focused on whether techniques to recellularize the natural templates of these tissues with human embryonic stem cells would result in comparable outcomes or would differ based on the tissue of origin. Results showed that elements remain within the scaffolds that could have an impact on transplant efficiency, and that recellularization of the tissues resulted in structures that were specific to either the kidney or to the lung.

Scientific Abstract:
Initial steps in establishing an optimal strategy for functional bioengineered tissues is generation of three-dimensional constructs containing cells with the appropriate organization and phenotype. To effectively utilize rhesus monkey decellularized kidney scaffolds, these studies evaluated two key parameters: (1) residual scaffold components after decellularization including proteomics analysis, and (2) the use of undifferentiated human embryonic stem cells (hESCs) for recellularization in order to explore cellular differentiation in a tissue-specific manner. Sections of kidney and lung were selected for a comparative evaluation because of their similar pattern of organogenesis. Proteomics analysis revealed the presence of growth factors and antimicrobial proteins as well as stress proteins and complement components. Immunohistochemistry of recellularized kidney scaffolds showed the generation of Cytokeratin+ epithelial tubule phenotypes throughout the scaffold that demonstrated a statistically significant increase in expression of kidney-associated genes compared to baseline hESC gene expression. Recellularization of lung scaffolds showed that cells lined the alveolar spaces and demonstrated statistically significant upregulation of key lung-associated genes. However, overall expression of kidney and lung-associated markers was not statistically different when the kidney and lung recellularized scaffolds were compared. These results suggest that decellularized scaffolds have an intrinsic spatial ability to influence hESC differentiation by physically shaping cells into tissue-appropriate structures and phenotypes, and that additional approaches may be needed to ensure consistent recellularization throughout the matrix.